UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/723,314	11/26/2003	Hanshermann Franke	30572/39753A	6830

4743 7590 04/06/2009

MARSHALL, GERSTEIN & BORUN LLP
233 SOUTH WACKER DRIVE
6300 SEARS TOWER
CHICAGO, IL 60606-6357

EXAMINER	
CHOI, FRANK I	
ART UNIT	PAPER NUMBER
1616	

MAIL DATE	DELIVERY MODE
04/06/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/723,314	FRANKE ET AL.	
	Examiner	Art Unit	
	FRANK I. CHOI	1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 January 2008 and 25 April 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-19,21 and 23-45* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-19,21 and 23-45* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *4/2/2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claim Objections

Claims 6-16, 23,28,30, 33-37 are objected to because of the following informalities:

Claims 6-16, 23,28,30, 33-37 use period marks in the body of the claim. Periods may not be used elsewhere in the claims except for abbreviations. See Fressola v. Manbeck, 36 USPQ2d 1211 (D.D.C. 1995). Further, if the Applicant intends to retain the identification of subparagraphs by using letters, the Applicant should not interchange uppercase and lowercase letter for the same component. Also, the applicant delete component e but claim 9 then refers to f and g instead of e and f. Since, the claims do not seems to use the letters as shorthand to avoid having to rewrite the subject matter in dependent claims, the Examiner suggests that they be removed from the claims altogether.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-19, 21, 23-45 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The nature of the invention:

The claim invention is directed to pharmaceutical compositions, methods of preparation and methods of treatment in which the composition contains oxcarbazepine having a specified particle size distribution and release rate resulting, in some of the dependent claims, in the specified plasma concentration of the oxcarbazepine and metabolite monohydroxydihydrocabamzepine. Claim 23 claims a capsule or pouche containing said oxcarbzepine which wasw mixed with other excipients and compacted and screened such that the screen material has the claimed particle size distribution.

The state of the prior art and the predictability or lack thereof in the art:

The prior art discloses tablets containing Trileptal ® (600 mg oxcarbazepine), HPMC, silica, magnesium stearate, crosspovidone in the core and a coating of HPMC, dye, PEG, talcum and titanium dioxde (WO 01/32183 (Norvartis) Pages 13, 14). Although, the Applicant's specification does not indicate the formulation of the comparative tablet, the Specification indicates that the tablet containing 600 mg oxcarbazepine was customary in the trade (Trileptal of the company Norvartis). As such, the Examiner assumes that the above tablet was what was tested. As such, although the prior at tablet contained the same amount of oxcarbazepine, the excipients, formulation process, etc. resulted in a different release rate and plasma concentration. Further, this is supported by other prior art which indicates that coatings and matrix characteristics, particle size, diluents, disintegrants, binders, granulating agents, lubricants, methods of granulation and compression (compression force has a significant influence on disintegration and particle size) on dissolution rates (Remington's (18^{th} Ed. 1990), page 1684, Remington's (17^{th} Ed. 1985), pages 655-658). Further, WO 2007/089926 discloses particles of oxcarbazepine with a d(0.1), d(0.5) and d(0.9) of about 21,71, and 248 microns, respectively,

which is bioequivalent to Trileptal ® (Page 17, lines 27-30, page 20, lines 18-30). Further, it is recognized in the art that USP paddle apparatus leads to high variability and unpredictablity in drug dissolution results and due to accumulation of disintegrated material at the bottom of the vessel the USP paddle apparatus provides an inaccurate reflection of drug release characteristics. e.g. fast release products may appear as slow release-products and bioequivalent products may appear to be bioinequivalent, having significantly different in vitro release characteristics (page 271). As such, predictability in the art is low as to what combination of ingredients and dosage formulations will result in the claimed release profile and plasma concentration.

The amount of direction or guidance present and the presence or absence of working examples:

The only example tested was a tablet containing 600 mg oxcarbazepine, ammonium methacrylate copolymer, sodium carboxymethyl starch, magnesium stearate and microcrystalline cellulose, however, the compression force is not disclosed, the tablet has no coating and there is no indication that the oxcarbazepine or compacted material containing said oxcarbazepine had the claimed particle size distributions (Specification, paragraphs 0055-0062). WO 03/101430 which is related to the present application discloses the exact same tested tablet, testing procedures and the same release profile and plasma concentration, however, unlike the present Application there is no disclosure relative to particle size distribution (WO 04/101430, pages 9-11). The English language version is US 2004/0185095. As such, there is no evidence that the claimed particle size distribution will result in the claimed release profile and plasma concentration.

The breadth of the claims and the quantity of experimentation needed:

The claims are broad in that the claims 1-5, 18,19, 21, 41, 42 are generally only limited by the particle size distribution of and release rate of oxcarbazepine, claims 6-17, 23-40, 43,44 indicate various additional ingredients, however, the compression force is not disclosed with respect to the tablets and some of the claims are directed to capsules or pouches. Given that particle size, compression force, the presence of excipients, etc. affect dissolution and plasma concentration and the only example tested was a tablet formulation having no coating, specific amounts of active agent and excipients in which the compression force was not disclosed, one of ordinary skill in the art would be required to due undue experimentation in order to determine what combination of compression force, particle sizes, core excipients, coatings and coating excipients, dosage forms (powders, granules, encapsulated powders and granules, sustained release forms, capsules, pouches, etc.) and formulation processing steps, will result in the claimed release profile and plasma concentration.

The Examiner has duly considered the Applicant's arguments and Declaration of Peter Lennartz (1/16/2008) but deems them unpersuasive.

The Applicant argues that the release profile can be predicted based on the particle size distribution regardless of the excipients. However, WO 2007/089926 also contains particles having a distribution falling within the scope of the claimed invention but the product is bioequivalent to Trileptal ®. Further, as indicated above, the claimed USP paddle method provides high variability, unpredictability and false results. As such, contrary to the Applicant's arguments, one of ordinary skill in the art would be required to do undue experimentation in order to determine what other combinations of excipients in combination with the claimed sized distribution of oxcarbazepine particles would result in the claimed dissolution profile.

Conclusion

A facsimile center has been established in Technology Center 1600. The hours of operation are Monday through Friday, 8:45 AM to 4:45 PM. The telecopier number for accessing the facsimile machine is 571-273-8300.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Frank Choi whose telephone number is (571)272-0610. Examiner maintains a compressed schedule and may be reached Monday, Tuesday, Wednesday and Thursday, 6:00 am – 4:30 pm (EST).

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's Supervisor, Johann R. Richter, can be reached at (571)272-0646. Additionally, Technology Center 1600's Receptionist and Customer Service can be reached at (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Frank Choi
Patent Examiner
Technology Center 1600
April 6, 2009

/Johann R. Richter/
Supervisory Patent Examiner, Art Unit 1616